

Remarks

Claims 12-29 are pending in the subject application. By this Amendment, Applicants have canceled claim 13 and amended claims 12, 14 and 15. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 12 and 14-29 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Applicants gratefully acknowledge the Examiner's indication that the species election has been withdrawn.

Claims 12-29 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants respectfully assert that the claims as filed are definite. However, in order to expedite prosecution of the subject application, by this Amendment, Applicants have incorporated an active method step in accordance with the Examiner's suggestion. Claim 12 has been amended to recite that the effective amount is sufficient to reduce or treat the rate of gamete numerical chromosomal alteration in the male. Support for this amendment can be found, for example, at page 9, lines 15-25 of the specification as originally filed. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 12-29 are rejected under 35 U.S.C. § 112, first paragraph, as nonenabled by the subject specification. Applicants submit that the currently pending claims are enabled. Applicants note that the Office Action presents a number of references that are argued to provide teaching that ones skilled in the art would not have expected the administration of a therapeutically effective amount of FSH to a male individual in need of treatment of gamete numerical chromosomal alterations to be effective. However, Applicants note that the as-filed specification provides teaching that that such a treatment protocol is effective for the treatment of gamete numerical chromosomal alterations in a male and that the observed effects are statistically significant. It is further noted that the Office Action criticizes the data presented in the Examples on the basis that "the examples are flawed in that there are no controls" (Office Action at page 4). In this regard, Applicants note that the treated population was also utilized as the "control population" in that the variation of the percentage of total aneuploidy, diploidy and total disomy for each of the treated populations was

measured at the different stages of the treatment regimen, i.e. 45 days before the treatment (-45); the day of the treatment (0); and 90 days after the beginning of the treatment (90)(see, for example, Figures 1-3; Brief Description of the Figures; and Example 2). Thus, it is respectfully submitted that the alleged flaw identified in the Office Action is, in fact, not present.

Applicants also note that the enablement requirement is satisfied if the specification describes any method for making and using the claimed invention that bears a “reasonable correlation” to the entire scope of the claims. *In re Fisher*, 427 F2d 833, 839; 166 USPQ 18, 24 (CCPA 1970). Claim 12 has been amended to recite a method for the reduction and/or treatment of gamete numerical chromosomal alternations in a male, comprising administration of an effective amount of FSH or FSH variant to a male in need thereof, wherein the effective amount is sufficient to reduce or treat the rate of gamete numerical chromosomal alteration in the male. Examples 1-4 of the specification demonstrate a statistically significant reduction in diploidy and aneuploidy in human male patients. Applicants submit that the claims as amended are commensurate in scope with the evidence provided in the specification. Applicants respectfully assert that the claims as filed are enabled. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 12-27 and 29 are rejected under 35 U.S.C. § 102(b) as anticipated by Foresta *et al.* (2002). In addition, claims 12-17, 19-27 and 29 are rejected under 35 U.S.C. § 102(b) as anticipated by Acosta *et al.* (1991). The Office Action indicates that the preamble of the claims is not accorded patentable weight, since there is no active method step. As indicated above, by this Amendment, Applicants have incorporated an active method step. Claim 12 has been amended to recite a method for the reduction and/or treatment of gamete numerical chromosomal alternations in a male, comprising administration of an effective amount of FSH or FSH variant to a male in need thereof, wherein the effective amount is sufficient to reduce or treat the rate of gamete numerical chromosomal alteration in the male. As acknowledged by the Examiner at pages 8 and 9 of the Office Action, Foresta *et al.* and Acosta *et al.* are silent with respect to patients having chromosomal abnormalities such as sperm diploidy, disomy, and aneuploidy.

As the Examiner is aware, in order for a claimed invention to be anticipated under 35 U.S.C. §102(b), all of the elements of the claim must be found in one reference. *Scripps Clinic & Research*

Foundation v. Genentech Inc., 927 F.2d 1565, 1576; 18 USPQ2d 1001, 1010 (Fed. Cir. 1991). Applicants respectfully assert that the *Foresta et al.* and *Acosta et al.* references do not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) is respectfully requested.

Claim 28 is rejected under 35 U.S.C. § 103(a) as obvious over *Acosta et al.* (1991) as applied to claims 12-17, 19-27 and 29 above and further in view of *Bouloux et al.* (2001). Applicants respectfully traverse the rejection.

The Office Action indicates that the preamble of the claims is not accorded patentable weight, since there is no active method step. As indicated above, by this Amendment, Applicants have incorporated an active method step. Claim 12, from which claim 28 depends, has been amended to recite a method for the reduction and/or treatment of gamete numerical chromosomal alternations in a male, comprising administration of an effective amount of FSH or FSH variant to a male in need thereof, wherein the effective amount is sufficient to reduce or treat the rate of gamete numerical chromosomal alteration in the male. As acknowledged by the Examiner at page 9 of the Office Action, the *Acosta et al.* reference is silent with respect to patients having chromosomal abnormalities such as sperm diploidy, disomy, and aneuploidy. The *Bouloux et al.* reference, which teaches that FSH, and potentially FSH-CTP, is safe and effective for treatment of infertility, does not cure the defect of the *Acosta et al.* reference. Moreover, at page 4, the Office Action indicates that the art teaches that elevated FSH levels in males is correlated with high levels of sperm chromosomal abnormalities, and thus “does not suggest to one of skill in the art that treatment of these disorders can be achieved by administering more of the very substance to patients that they have too much of.”

Applicants respectfully assert that the claimed invention is not obvious over the cited references. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants’ agreement with or acquiescence in the Examiner’s position. Applicants


expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

A handwritten signature in black ink, reading "Frank C. Eisenschenk". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Frank C. Eisenschenk, Ph.D.

Patent Attorney

Registration No. 45,332

Phone No.: 352-375-8100

Fax No.: 352-372-5800

Address: P.O. Box 142950
Gainesville, FL 32614-2950

FCE/jb/sl